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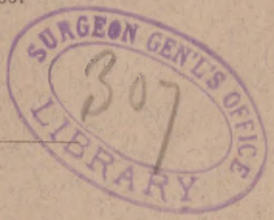
A CONTRIBUTION

TO THE STUDY OF

THE TUBERCLE-BACILLUS.

By HAROLD C. ERNST, M.D.
OF JAMAICA PLAIN.

Read at the Annual Meeting of the Massachusetts Medical Society,
June 12, 1883.



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Koch's (1)[1] announcement in the Spring of last year of his discovery of the specific organism lying at the bottom of and being the cause of tuberculosis, marks an epoch in the history of this much-discussed pathological problem such as it had never known before.

Beginning with Villemin's (2) experiments tending to show the inoculability of tubercle, this subject has attracted attention from the best observers of the time ever since, and their results have tended more and more to show the communicability of the disease. The strides of microscopic pathology and the facts observed in regard to micro-organisms in other forms of disease, have assisted in preparing scientific minds for the discovery that is under consideration to-day.

The importance of Koch's facts has led to an immense amount of work in the same direction, for purposes of confirmation or refutation. It is now more than a year since his results were first given to the public, and a review of what has been done since then will be of interest and importance. No discussion of the individual papers will be attempted, and only those will be mentioned which have for their object the determination of the existence of the tubercle-bacillus and its significance.

Koch's results—after a long series of experiments, in

[1] See references at the close of this paper.

which he not only discovered the organism which he claimed to be the actual cause of tuberculosis, but proved the assertion by the most careful cultivations and inoculations—are now so well known as to require little comment here.

Since the publication of his experiments, investigations have been carried on with a view to the discovery of the tubercle-bacillus in all the morbid processes known as tuberculous. In all of these experiments, the proportion of success to failure has seemed to grow larger as observers have become more familiar with the manipulation necessary for the demonstration of the bacillus. The few who have directly denied its existence in the tissues, or its pathological significance if there, have either seen reason to change their views or are still at work upon the problem. Before Koch, there were other observers claiming the discovery of the specific cause of tuberculosis—thus: as the result of his work, Klebs (3) had announced his monas tuberculosum—an actively-moving organism; Schüller (4) and Toussaint (5), a spherical micrococcus; and Aufrecht (6) speaks of a rod-shaped organism, which he found in the centre of tuberculous masses and which he now claims to be identical with Koch's bacillus.

From all of these, Koch's discovery differs, in that it has no movement, is rod-shaped, and more than twice as long as it is broad—being from one-quarter to wholly as long as the diameter of a red blood-corpuscle—and in that he has isolated his discovery by cultivation and has produced the specific disease with the result—which none of the others have ever done.

Entering now upon the discussion of the papers that have been brought out by Koch's work, we come first upon that of Machiafara and Celli (7), who published results showing that they had found the bacilli in fifteen cases of phthisis—one with hæmoptysis and no physical signs—and in the

stools of phthisical patients in great numbers. They examined also, and with negative results in every examination, thirteen cases of other lung-disease.

Formad (8), after what he considers exhaustive research, grants that bacilli are present, but not invariably: he thinks that they may be the *causa mortis* by producing a fatal result in a process which would otherwise not be so, but he does not ascribe to this organism any quality which would make it a veritable *causa* or *materies morbi*.

Balmer and Fräntzel(9) find the bacilli in enormous numbers in rapid cases of phthisis, and less numerous in the more chronic ones. "Infection fever" was always present in the cases in which bacilli were present in large numbers. They found bacilli very numerous in the tissue of tuberculous lung, in the walls of tuberculous ulcerations of the intestines, and in the pus of tuberculous joint affections. Their observations lead them to the following conclusions:—They found the tubercle-bacillus in the sputum of one hundred and twenty cases of phthisis without exception. In the cases of lung disease not tuberculous, tubercle-bacilli were never found. Therefore when they are found in the sputum we have a case of tuberculosis. On the other hand, when they are absent after repeated and careful examinations of the sputum, tuberculosis of the lung may be excluded. They consider that a perfect prognosis of a case may be given as the result of repeated examinations of the sputum extending over a period of weeks or even months. They also conclude that the most favorable soil for the growth of this bacillus is in the cheesy contents of a cavity rather than in its walls.

Hiller (10) thinks it possible to formulate the dogma that "Initial hæmoptysis is a symptom of the infection of the lungs, standing in the relation of effect to cause."

Schmidt (11) thought he had proved that the so-called tubercle-bacilli were fat crystals—because they disappeared

if treated with ether. Hirschfelder (12) has however shown that even after boiling the cover-glass in ether, and washing in fresh ether, the bacilli may be readily demonstrated by Ehrlich's method. Schmidt probably dissolved out the coloring matter, and has himself since come to a belief in the bacillus.

Ransome (13) demonstrated the bacilli in the expired air of cases of undoubted phthisis.

An opponent of Koch's views on the specific nature of the tubercle-bacillus is Balogh (14), who says he has found bacilli in the marshes around Pesth, which are indistinguishable from the tubercle-bacillus. Inhalation experiments with these bacilli caused nodular growths in the lung in which the tubercle-bacillus was found; and inoculation with scarlatinal urine and with bronchial sputum gave the same nodular growths. He took no measures—so far as reported—for the absolute exclusion of the tubercle-bacillus.

Prof. Koryani (15) found Koch's bacilli in the sputum of a case which had been regarded as one of pulmonary syphilis; by this means a correct diagnosis was reached.

Guttman (16) has been unsuccessful in his researches, only finding the bacilli four times out of one hundred preparations of phthisical sputum—all prepared after Ehrlich's method.

D'Espine (17) finds no correspondence between the number of the bacilli and the stage of the disease.

Lichtheim (18) has found bacilli in the sputum of patients with cough, before the lungs present any sign whatever. He considers, however, that the point of origin of inflammation must have some communication with the air passages before the bacilli can be discovered in the sputum, even in well advanced tuberculosis. He found bacilli in the stools of intestinal tuberculosis, and especially in the ulcerations of the intestinal wall—he also found them in cases of tuberculous peritonitis.

Chiari (19) thinks that the number of the bacilli is in direct proportion to the severity of the disease. He has never found any other bacilli staining as does Koch's.

Heron (20) believes that the tubercle-bacillus furnishes a good prognostic guide, and that the more numerous it is, the more rapidly fatal is the disease.

Smith (21) demonstrated the tubercle-bacillus in the expired air of consumptives.

Pfeiffer (22), after a great number of observations, comes to the conclusion that the bacilli can always be found in the sputum of advanced tubercular disease of the lung, but that the examination must be repeated a great number of times before the definite exclusion of bacilli can be reached.

Babès (23) of Pesth demonstrated the bacilli in the urine of three patients, in two of whom tuberculous nephritis with ulceration of the pelvis of the kidney was demonstrated afterwards in post-mortem examination; in one there was also tuberculous ulceration of the bladder.

Crämer and Menche (24, 24*) both consider the tubercle-bacillus as a diagnostic landmark. Crämer, however, found an organism staining like the tubercle-bacillus in every case in twenty examinations of healthy stools. Menche claims that the examinations are liable to error because of imperfect staining—and further, that possibly tuberculosis of the intestinal wall may be only manifest in the stools.

Fränkel (25) found numerous tubercle-bacilli in the pus of a scrofulous- or tuberculous-joint, and Dreschfeld (26) confirms this by the same observation in a case of the same nature in the ankle. Fränkel has also found the bacilli in the secretions covering laryngeal ulcers in fifteen out of sixteen cases. Lewin confirms this, but Guttman was unable to do so in two cases.

Ziehl (27) has obtained positive results in seventy-three cases of undoubted phthisis; he found no bacilli in thirty-four cases of other lung disease. He thinks it more likely that

there is no other "fungous-form" in nature to be stained thus, than that the tubercle-bacillus is the only one which is stained slowly in Fuchsine and Methylene-blue. He considers the observation of the bacillus a certain means of diagnosis of the tuberculous process and a method of differentiation from other forms of disease; but their absence must not be considered as excluding tuberculosis. He speaks with especial certainty upon the prognostic value of the numbers of the bacilli in the excretions.

Rosenstein (28) found the bacillus in the urine of a patient with symptoms of tuberculous disease of the epididymis—the lungs being perfectly free. Lichtheim detected the bacillus, post mortem, in the contents of the pelvis of the kidney in a case of renal tuberculosis.

West's (29) conclusions, after the examination of fifty cases of phthisis, are: I. That bacilli are found in all cases of phthisis with excavations, varying in number with the rapidity of the destructive process; II. That their arrangement in groups and masses indicates a greater amount of destruction of the lung tissue, unless the isolated bacilli are in great numbers; III. That there is no variation in the size of the bacilli; IV. That the bacillus being evidence of the destruction of lung tissue may be confirmatory diagnostic evidence, although he has only found them after the physical signs were clear.

Williams (30) found bacilli in one hundred and six out of one hundred and nine cases of phthisis. Of the remaining three—in one, but one examination was made; in another, the excretion seemed to be purely bronchial; and in the third, the slides were spoiled and he could get no more. He considers it hardly justifiable to draw any conclusions from the activity of the disease and the number of the bacilli —although as a rule they are few in the cases in which the disease is quiescent.

Dreschfeld (26) found bacilli in varying numbers in forty-

six cases of positive lung-tuberculosis; in two or three doubtful cases; and none in eight non-tuberculous lung affections. He considers them of diagnostic but not of prognostic value.

Dettweiler and Meissen (31), after the examination of eighty-seven cases of phthisis, conclude that the number of the bacilli in the sputum has no bearing upon the prognosis. An observation which they have confirmed by a series of parallel records—clinical and of the number of the bacilli in the sputum.

Spina (32) asserts that there are other bacilli with the same staining reaction as the tubercle-bacillus, and that he can find no other means of differentiation; that he could not find Koch's bacillus in tuberculous organs that had not been for a certain time exposed to the air; and that Koch's results are inconclusive, on the ground of too few experiments.

Immediately after Spina's work was published, Koch's(33) reply to his critics appeared. His article is characterized by vigor and by an evident security in the position he took at the start upon the merits of his discovery.

He first turns his attention to America, and merely mentions Cutter(34), who considers the bacillus to be "embryonal forms of mycoderma aceti." Of Rollin Gregg (35), who suggests that the bacillus may be only fibrine filaments, Koch says he seems to have considered that microscopical investigations would be superfluous for the establishment of his views. Schmidt (11) is advised to get good colors and learn how to use them before announcing fat crystals as bacilli. Formad (8) is told to become sufficiently expert not to let his animals die of tuberculosis when inoculated with wood, glass, metal, &c. Sternberg's (36) failure to find the bacillus puts him out of court.

Then turning to Germany, he remarks that "if one thinks that Germany cannot bring forth such blossoms of tubercle

literature as these, he is much mistaken." He says that Beneke (37) must have found fat crystals and not bacilli in the blood of healthy men; that Crämer's twenty cases of bacilli in the stools of healthy men have been contradicted by Menche (24[a]) and Gaffky's (38) experiments, and that they were not identified with the tubercle-bacillus, although they were stained after Ehrlich's method. Balogh (14) found bacilli in Berlin mud, which Koch did not succeed in doing. Koch moreover denies any value to Balogh's inoculation experiments, because no sufficient precautions for the exclusion of the tubercle-bacillus were taken. Schottelius (39) produced anatomical tuberculosis in dogs by causing them to inhale masses of finely-pulverized non-tuberculous matter. Koch says that the anatomical appearances are not the criterion of what is tuberculous, and that Bertheau and Weigart have completely contradicted him. Dettweiler (31) discriminating between phthisis and general tuberculosis, attempts to show that the tubercle-bacillus is the accompaniment and not the cause of tuberculosis. Koch thinks he would change his mind if he knew more about the pathology of tuberculosis. Koch (32) then turns his attention to Spina, and in summing up a criticism of his work—after leaving exposed the fallacy of his reasoning—concludes by saying: "All his work shows that Spina does not know enough to observe bacteria microscopically, nor to cultivate nor to inoculate them. His work will have no influence upon the discovery of the tubercle-bacillus."

Since Koch's article in March, observations have been published by

Demme (40), who thinks he can confirm Lichtheim's observations as to the bacilli in acute miliary tuberculosis. He considers it probable that ulceration is necessary before the bacilli can be seen in the excretions. As an instance of probable infection, he relates the case of a child which was put out to nurse in a family, and whose foster-father

died of acute phthisis. The child had not the slightest hereditary taint of phthisis or of syphilis, and was infected through the nasal mucous membrane. After suffering from ulcerative ozæna, it developed tubercular meningitis, and died. Tubercle-bacilli were found in the ulcerated and non-ulcerated pituitary membrane.

Purser (41) quotes a case in which the bacilli were discovered in the sputum five weeks before the clinical signs showed any disease of the lungs.

Prudden (42) found bacilli in forty-six out of fifty-eight cases, in simple sputum preparations; and in thirty-nine out of forty-two, of sections. He thinks it is evident that, in nearly every case of tuberculosis, there are many miliary tubercles of all forms, and in many cases, much tuberculous tissue from which the bacilli seem to be entirely absent —which may perhaps be explained by their not staining well after life is gone or going, and perhaps by their having disappeared from tubercle which has come to a standstill.

The longest and clearest work upon the subject of the tubercle-bacillus yet published is that by Mr. W. Watson Cheyne (43). As a preliminary to his work, this gentleman visited the laboratories of Toussaint at Toulouse, and of Koch at Berlin, and observed the methods of work at both places—carrying away material for subsequent experiment and examination.

In his experiments as to the inoculability of tuberculosis he has exercised the greatest possible care to prevent contamination of instruments and hands, and has kept the animals experimented upon under the very best hygienic conditions—this latter a precaution that has not always been taken.

In his inoculation experiments with non-tuberculous material, he obtained negative results in every case. He explains the contradictory results of former observers by:— first, the mistaking of cheesy masses, not tubercular, for tu-

bercle, where a microscopic examination was not made; and, second, by the fact that even where a microscopic examination was made, the accuracy of the diagnosis would depend very greatly upon the methods of staining employed and the views which the observer held as to what constituted a tubercle. It must be remembered also, with regard to the early experiments in this direction, that the danger of mediate inoculation was not recognized, and that therefore the channels for the possible introduction of specific micro-organisms were left unguarded—as the precautions necessary for the thorough disinfection of instruments, etc., had not yet been made out. He failed to obtain tubercle with the material obtained from Toussaint, and explains the latter's results by the growth of tubercle-bacilli in his culture-fluids and their introduction during inoculation. The latter occurrence is rendered more probable because Toussaint trusts so much to disinfection by carbolic acid, which, although effectual against ordinary micro-organisms, has been shown to have no effect upon the spores of other bacilli, unless it acts for a long time. The tubercle-bacillus apparently produces spores, and there is no reason to suppose that these are less resistant than those of bacillus anthracis and other bacilli.

In the researches of Klebs and Schüller, a pure cultivation was not obtained, nor were the cultivations carried beyond the third generation; nor was Schüller always successful in producing tuberculosis by the injection of his cultivations. Not even the best microscopists and those who have done most with micro-organisms (Koch, Weigert, etc.) have been able to find the micrococci which Schüller declares he has seen in artificial tuberculosis. Cheyne has found micrococci only twice, and neither time in tubercle.

The difference between the results of previous researches and Koch's is that his are much the more definite. He, like others, cultivates micro-organisms from tubercle, but

now it is no longer the fact that he only sometimes succeeds in causing tuberculosis, and that the tubercle thus produced occurs as slowly or more slowly than after the inoculation of tuberculous material. The result of the inoculation of his cultivations is certain, and more rapid in its commencement than after the inoculation of tuberculous matter.

As a result of all his work, Cheyne comes decidedly to the conclusion that the tubercle-bacillus is the cause of tuberculosis, and that scrofulous glands, degenerated (strumous) synovial membranes of joints, phthisical lungs—in short, all those materials obtained from man, which, inoculated into animals, produce acute tuberculosis—contain in them bodies (bacilli) which, if they entered the circulation in sufficient numbers, would give rise to acute tuberculosis. It has been demonstrated by several observers that probably in all cases of acute tuberculosis a place can be found where these bacilli get into the circulation.

Cheyne considers the bacilli to be developed in the first instance in epithelioid cells, and that, in the lung, these cells are derived from the alveoli. He thinks that giant cells are epithelioid cells which have grown rapidly—apparently as the result of the presence of bacilli in them. He thinks that the structural definition of a tubercle must run as follows:—

"A nodule, composed of a central mass, consisting in the main of epithelioid cells, or in its place a cheesy mass, surrounded by more or less inflammatory tissue, with or without the presence of giant cells. The absolute diagnostic mark is the presence of the tubercle-bacillus. It is not, however, always necessary for a tubercle to be a nodule. If there are plenty of epithelial cells, or if it occurs when there are no pouches—as there are in the lung—it may be diffuse."

Cheyne then discusses the facts of the varying numbers of the bacilli in phthisis, and draws the conclusions that

according to the number and rapidity of growth of the bacilli we have fibroid phthisis or caseous pneumonia. On this basis can also be explained the difference in the effects produced by these organisms in man and rodents. Rodents which are inoculated subcutaneously always develope general acute tuberculosis, which is extremely rare in man when compared with the frequency of pulmonary tubercle; because in man the bacilli are not inoculated, but are received into the bronchial tubes by inhalation; their entrance into the circulation is prevented in the first place by the inflammatory changes which occur around the alveoli in which the bacilli grow. If man were inoculated as rodents are, analogy makes it probable that acute tuberculosis would be developed.

The papers which have appeared since this publication are few but of great importance.

Ransome (44) has shown bacilli exhaled by a patient suffering from phthisis. He obtained them by condensing the vapor of the breath in a large glass globe surrounded by ice and salt, and stained them by Gibbes' (44[a]) method.

Cornil (45) studied the bacillus in tuberculous granulations as being the most simple lesions. He found generally in the centre of a tuberculous mass a vessel obliterated by fibrin, and bacilli in the centre of this: they were usually present also in the walls of this vessel and near by, in varying numbers. He found that the number and dissemination of the bacilli varies very greatly, and could not find them at all in one case of tubercular meningitis. He found them in the spaces between the epithelial cells (lymph-spaces of Ranvier), and in the connective tissue, and in the protoplasm about the nuclei of the embryonal cells which form tubercle.

Ballagi (46) concludes from his investigations that:—1.—Koch's bacillus can be separated from other forms of bacilli. 2.—A differential diagnosis from all other organisms

can be reached by their staining reaction (Ehrlich's), and they can be thus separated in the tissues from putrefactive and disease germs (as the bacillus of leprosy). 3.—Putrefactive and other bacteria cannot be isolated by any known special staining method. 4.—The tubercle-bacilli do not occur with regularity in the sputum of persons in the first stages of phthisis (apex catarrh, hæmoptysis). 5.—In the sputum from patients in the advanced or fibroid stages the bacilli can always be found, especially in the form known as galloping consumption, although in no case do their numbers correspond invariably with the height of the fever or the stage of the destructive process. 6.—The tubercle-bacilli can be found in tuberculous organs when the process is not very old (chronisch). 7.—There are no bacilli in the sputum of non-phthisical patients. 8.—Their repeated occurrence is conclusive of the diagnosis. Their absence, however, does not prove the absence of a tuberculous process. 9.—Their number and distribution is of no prognostic value.

Fräntzel (47) has now observed three hundred and eighty cases of phthisis, and followed them up for months. He has examined also eighty cases of other lung disease, and always with negative results. In every one of the cases of phthisis he found bacilli in the sputum, and was often able to make a diagnosis by their presence, when the physical signs were negative—a diagnosis which was invariably confirmed by the further progress of the disease. In five cases which progressed with the picture of phthisis, no tubercle-bacilli were found, and further observation showed that none of them were cases of "cheesy infectious phthisis" (which was confirmed in three by post-mortem examination). These further observations lead him to adhere to the first of the three laws which he enunciated in his former article—that the presence of the bacillus in the sputum determines the presence of tuberculosis. He also considers the

quantity of bacilli—as determined after repeated examinations extending over a long time—as of great prognostic value. (He thinks that the examination should be extended over weeks or months, and should be repeated every day—or at least every second day—with notes and comparisons, and the conclusions to be drawn from the general average.) He thinks that such a long series of observations will give us a more certain prognosis than even the physical signs. As a result of his further study of the subject, he wishes to modify, slightly, his second law, i. e., "that wherever, after repeated and careful examinations, no bacilli are found in the sputum, there is no tuberculosis of the lung." This law would now read as follows:—"When, after repeated and careful examinations, no bacilli are found —provided that sputum is present and comes from the lungs —there is either no lung tuberculosis, or else there are no cheesy softened foci emptying their contents into the bronchi."

At a medical meeting in Vienna, on May 13th, Spina (48) read a paper on the subject of Koch's bacillus. It was especially devoted to the discussion of its behavior towards staining fluids, and he still denies any specific property to it. He gives no further inoculation or cultivation experiments, and bases his rejection of Koch's theory especially upon the fact that the bacilli are found to act differently toward staining fluids than it was at first announced they did.

In proof of the presence of other organisms having the same staining reaction, he gives the results of Dr. Matray's work, which is as follows:—

1. Micro-organisms of many kinds, especially staff-shaped bacteria, cocci singly and in colonies, leptothrix and torula forms, were stained blue on a brown ground: *a*, in bronchiectic sputum; *b*, in sputum of bronchial asthma; *c*, in sputum of diffuse bronchitis (every time in 94 preparations); *d*, in the "furred tongue" of non-phthisical patients

(eleven cases with 28 preparations); *e*, in the lochia of non-phthisical lying-in women (twelve cases with 43 preparations); *f*, in the sputum of fourteen cases of pneumonia (46 preparations); *g*, in the stools of a typhus fever patient; *h*, in the expressed fluid of a case dead of malignant œdema.

2. Bacilli in form, size, grouping and reaction like the tubercle-bacilli were seen: *a*, in the sputum of a case of bronchiectasis (in 54 preparations); *b*, in the furred-tongue secretion of sick and well persons (eleven cases, 28 preparations); *c*, in the stools of a typhus-fever patient (every time in 16 preparations); *d*, in the sputum of a case of bronchial asthma (every time in 34 preparations); *e*, in the sputum of a case of diffuse bronchitis (6 preparations); *f*, in the lochia of a healthy lying-in woman (2 preparations); *g*, in a case of croupous pneumonia (4 preparations).

He quotes Kaberhel and Matray (assistants assigned to him by Stricker) as concluding that, "on the one hand, micro-organisms which do not differ from the tubercle-bacillus react to staining fluids as do these bacilli; and on the other hand, that Koch's bacilli react to staining fluids exactly as do other micro-organisms."

He also quotes, as a point against the specific nature of the tubercle-bacillus, the recent observation of a bacillus similar to these in several cases of lupus.

Stricker himself addressed this meeting in support of Spina and his methods.

Klebs (49) as the result of his more recent work, gives the following summary:—

1. The tuberculous process is caused by organisms, as was first shown by me, and rendered certain by R. Koch.

2. I have not come to the same results as Koch in regard to the morphological relations of the tuberculous organism. On the one hand, I must hold fast to the fact that

finely granular micrococci are present in the albumen cultures, as well as in the youngest form of inoculated tubercle. On the other hand, I am in no way meaning to assert that Koch's bacilli are unessential impurities. They appear to represent an essential stage of development of the tubercle organism for the further development of tuberculosis, if they are not always present.

3. In regard to the history of the development of tuberculosis, I think that I have presented the proof that:

(a) The development of the tuberculous process begins very soon after the inoculation, and not after from 10 to 14 days, as Cohnheim and others believe. The difference depends, not upon an error of these last investigators, but upon the nature of the changes, which are to be regarded as the first stage of the tuberculous process. Completely formed tubercles, which can be distinguished with the unaided eye, appear in fact only after the longer period. But before the appearance of these, there are already extensive cellular deposits present in places which are at a great distance from the place of inoculation (mesentery). These represent perivascular infiltrations which are either developed further to the known form of tubercles, or can retrograde in the different stages of their development (cheesy nodules, either with or without contracting cicatrization, adhesive and deforming forms of peritonitis).

(b) The same primary method of distribution is also found in human tuberculosis, in which also the traces of these retrogressive formations in the mesentery and omentum are found in cases of pulmonary tuberculosis. In other cases, on the contrary, a further development of this form of tuberculous invasion comes on, which leads to the formation of cheesy foci in the organs, which are only related by means of the blood-vessels with the point of entrance of the tubercular virus into the organism (cheesy foci of the bones, the central nerve-apparatus, etc.).

The work which I have done upon this subject has been for the purpose of identifying the bacillus, and determining the frequency of its occurrence in tuberculous lesions. The organs examined have been lungs, liver, spleen, kidney, peritoneum, bronchial, mesenteric and inguinal glands, pia mater and the eye. In all of these bacilli have been found in varying numbers. They are less numerous in old, or slow, processes; very abundant in rapid ones, and especially so in the cavities filled with cheesy material. They are found in the swollen epithelioid cells of tubercle, or lying between them—singly, or in groups of from two to a dozen or more. They very frequently seem to be divided into a series of dots, from four to six in number, which occupy the body of the staff, and are taken to be spores. The result of my observation is confirmatory proof of the existence of the bacilli, and of Cheyne's proposition that their presence is diagnostic of tubercle. The difficulty with which they have been demonstrated in some cases, and the care required to obtain the desired result, seem to explain some of the failures in this direction. Nothing less than a $\frac{1}{12}$ Zeiss objective, together with an Abbé's illuminator, is sufficient for the perfect examination of a section. All my observations have been made with this apparatus, and a No. 3 eyepiece. All the sections have been made with a Jung microtome. Upon several occasions the bacilli have been observed in the blood-vessels, which would seem to show one method of auto-infection—the lymph-channels undoubtedly furnish another. I have seen a bacillus lying half in, half out of a swollen cell, its presence seeming to have acted as an irritant upon this special cell element. I have never seen anything but the bacillus staining red on a blue ground—although there have been plenty of other organisms which were stained blue.

The method of staining employed has been practically that of Ehrlich, which has seemed to give the most satisfactory results. It is as follows:

For sputum:—The cover-glasses are spread with a thin layer, taken from the more solid portion of the specimen, using fired platinum needles for its distribution. They are then dried carefully over the flame of an alcohol lamp, and after drying are passed two or three times through the flame itself. They are then placed in a solution of Fuchsine B. and aniline oil—one gramme of the first to fifty grammes of the second. The latter is made by shaking a few drops of aniline oil with distilled water and filtering. The specimens are allowed to stand in this solution for twenty-four hours. They are then washed and placed in a solution of one part of nitric acid (C. P.) and two parts of distilled water, and allowed to remain until they are completely decolorized, or until at the most a pinkish hue is all that is left visible to the eye. All the acid is then removed by repeated washing in distilled water, and the specimens are placed in a saturated watery solution of methyline-blue and allowed to remain for from five to eight minutes. The superfluous staining-fluid is then removed by repeated washing, the specimens are carefully dried as before, and are finally mounted in Canada balsam and examined.

For the tissues a similar method was pursued, except with the differences made necessary by their nature. Before placing in the Fuchsine solution, the alcohol should be removed by thorough washing, and the reagents should be allowed to act for a longer time, more especially when the sections are thick or the specimens are old. After staining in methyline-blue, they should be washed, dehydrated in alcohol, cleared up in oil of cloves, and mounted in Canada balsam.

The following is a complete record of the examinations I have made of different organs for the detection of the bacilli:

No. I.—A guinea-pig inoculated in the groin with a few drops of tuberculous sputum, in December, 1882; died in the middle of January, 1883.

Sections were prepared from the liver, spleen and peritoneum,—the lungs were healthy.

No bacilli were found in the sections of the liver.

The spleen showed bacilli singly in the tissues and in the swollen epithelial cells.

The peritoneum containd bacilli in the miliary nodules, about the edges, and in the centre of the tuberculous mass.

No. II.—A guinea-pig inoculated in the same manner as the preceding; died January 13, 1883.

No changes in any organ but in the liver.

Slides from this showed the bacilli in numerous places in and near the tuberculous portion, which was in the form of infiltration, rather than of nodules. The general position of the bacilli was in the lymphoid cells, and rather in the region of the portal vein.

No. III.—A guinea-pig inoculated as the preceding, in December, 1882; died in March, 1883.

The lungs presented no abnormal appearances.

The spleen showed plenty of evidence of degeneration, and bacilli were found in numbers in the cells and lying free in the tissues.

The liver and an enlarged inguinal gland were examined, with negative results.

No. IV.—A guinea-pig inoculated on March 13, with a few drops of tuberculous sputum (from Case IV.); the syringe was inserted in the left inguinal region just under the skin. Died in ten days.

All the organs gave negative results, except in the spleen, where, with no changes visible to the naked eye, a number of bacilli were found in and near the finer blood-vessels.

The cellular tissue at the point of inoculation was found to be stuffed with bacilli, lying in and between the much swollen cells, and in immense numbers.

No. V.—A guinea-pig inoculated in the same manner as the first three, in December, 1882; died, after progressive emaciation, on April 2, 1883.

All the organs showed tubercular infiltration, and sections under the microscope showed bacilli in the lungs, liver, spleen, kidney, inguinal glands, and skin under the point of inoculation.

No. VI.—A guinea-pig inoculated in the eye, in December, 1882; died April 15, 1883.

The lungs, liver and glands showed signs of disease.

The bacilli were found in plenty in the giant cells and the alveolar walls of the infected portion of the lungs, and in smaller numbers in the cells and lying free at the edges of the tuberculous deposit in the liver. They were also found in the gland examined.

No. VII.—A child of 3½ years, died of acute miliary tuberculosis.

Sections from the lung, liver and mesenteric gland showed bacilli very distinctly. Slides from the liver and peritoneum were unsuccessfully mounted and gave negative results.

No. VIII.—A cheesy bronchial gland, removed three months before examination, and preserved in absolute alcohol.

Bacilli were found in plenty in the cheesy portions near their edges; fewer in the degenerated parts, and scattered through the comparatively healthy tissue beyond.

No. IX.—A case of acute miliary tuberculosis in a child.

Sections from a peritoneal gland and the liver gave negative results; there was no tuberculous infiltration on the slides prepared.

The sections from the kidney contained very little tuberculous infiltration. Bacilli were noticed in small numbers in the region of the straight tubules, and a few in the interior of swollen Malpighian bodies.

The omentum contained occasional masses of bacilli, with numbers of isolated staffs in the infiltrated tissue.

No. X.—A specimen marked "Gland from Autopsy."

But two slides were prepared from it, and gave no evidence of the presence of bacilli.

The specimen was very old, and had no attainable history; it may therefore be fairly rejected as evidence.

No. XI.—Tuberculosis of lung.

A specimen of very old fibroid phthisis. The tissue under examination was almost all cicatricial, and nothing was seen that could be distinctly made out as the bacillus.

No. XII.—Tuberculosis of peritoneum.

The nodules were extremely fine and widely separated, and a section of one was not obtained. Bacilli were seen, however, in small numbers, lying singly in the tissues where the presence of swollen cells indicated the neighborhood of the tuberculous process.

No. XIII.—This was a specimen sent in as a "Cheesy Mesenteric Gland," from a case in which death was caused by the perforation of an ulcer of the intestine into the peritoneal cavity and the subsequent peritonitis.

There was no tuberculous disease of the gland at all, and bacilli were not found.

No. XIV.—Contents of a cheesy cavity from the lung of a rapidly fatal case of tuberculosis.

Bacilli were found in immense numbers; in some cases the cells seemed to be stuffed with them, and most of them showed a well marked division into spores.

No. XV.—Scrapings from the wall of a lung cavity in an ordinary case of phthisis.

Bacilli in immense numbers. In some places the whole field filled with them.

No. XVI.—Contents of a lung cavity in a case of slow tuberculosis.

Bacilli in immense numbers, in masses and singly, and presenting well-marked divisions into spores.

No. XVII.—Cheesy cervical gland.

Largely made up of fibrous material, with a few small cheesy foci. Bacilli were found in the edges of these portions in clumps and singly, and in the few giant cells that were seen.

No. XVIII.—Case of tubercular meningitis; dead after a month's illness.

A much enlarged bronchial gland was found, and the pia mater was full of minute granulations.

Bacilli were found scattered about near the edges of the tubercular portion of the gland, with many spores.

Sections of the pia mater showed very fine bacilli, with many spores—their situation being, in general, in the neighborhood of the finer blood-vessels and the lymph spaces. The origin of infection in this case was very evidently the enlarged gland.

No. XIX.—Tuberculous lung.

This specimen was a mass of tubercle, with cheesy foci and cavities.

The bacilli were found in the edges of the cheesy mass —in some instances in its centre. There were many spores, and occasionally bacilli were seen in what was apparently healthy tissue.

No. XX.—Tuberculous lung.

This, like the preceding, was a mass of tubercle, with many cheesy foci and much cicatricial tissue.

Bacilli were found, in not very large numbers, near the edges of the more recent degenerations; in much less abundance in the old fibrous portions.

No. XXI.—Tuberculosis of kidney.

Bacilli were found in plenty in the contents of a small cavity in the cortex of the kidney, and in the tissue from a nodule near by.

This case had been diagnosticated during life as a perinephritic abscess, and a drainage tube had been inserted for almost a year.

No. XXII.—Tuberculosis of eye.

This specimen was removed last fall, and had been preserved in chromic acid.

It was only after two attempts, and staining prolonged for

forty-eight hours, that a few bacilli were discovered in the nodule.

No. XXIII.—Acute miliary tuberculosis in a child.

Bacilli were found in large numbers in the cells in the tuberculous portions of the spleen, of an enlarged cheesy mesenteric gland, and in a tuberculous ulceration of the intestine.

As a result it will be seen that in every case of inoculation tuberculosis was developed, and the microscope revealed the bacillus in some portion of the organs of the animals experimented upon. There are a number of guinea-pigs still under observation. I was able to trace the bacilli with increasing certainty as practice trained my eye for their definition in the tissues. I have found a marked difference in the apparent size of these organisms in the sections examined. In some specimens they appear very fine and delicate—almost indistinguishable—sometimes only a line of dots being visible: in most cases they are exceedingly distinct and well-marked. However, as they are always of the same size and appearance in the preparations of fluid matter, and as those which appear to be finer and more delicate seem to fade quicker, I am led to believe that the apparent variations in size are due to optical effects from imperfect staining. Some observers obtained their results in the examination of tuberculous tissue by grinding a tubercle in a mortar with water, and drying the resultant mass upon cover-glasses in the manner of sputum preparations. The ease of this method is more to be commended than its accuracy—for in an examination of this kind every source of error should be eliminated that it is possible to get rid of.

In February last I began a series of observations of the sputum of a set of phthisical patients—all known to be so by the physical signs. These observations have been continued up to

very recently, and the results obtained in five represented in a diagrammatic manner upon the charts. The upper curve represents the temperature of the day of the examination—the lower, the number of bacilli. The examinations have been made at average intervals of a week. The results of the examinations of the sputum are here given in detail.

Case I.—Sick for three years—hæmoptysis the first symptom.

Thirteen examinations of the sputum were made, with positive results in eleven. The number of bacilli varied from none at all to very numerous. The results are condensed on Chart I.

Case II.—Sick for one year—hæmoptysis the first symptom.

From February 17 to June 3, fourteen examinations were made, with positive results in thirteen. When bacilli were found at all, they always occurred in large numbers. (Vide Chart II.)

Case III.—Cough for six months. Gained weight while under observation, and was finally discharged relieved.

From February 17 to April 20, eleven examinations were made, with positive results in six. For five successive examinations no bacilli were seen, and they never occurred in large numbers.

Case IV.—Cough for eight months.

From February 17 to April 20, ten examinations were made, with positive results in nine. The number of bacilli varied very greatly, and the results are tabulated on Chart IV.

Case V.—Sick for seven years.

From February 17 to June 3, fifteen examinations of the sputum were made, with positive results in nine; the bacilli always occurred in very small numbers. (Chart V.)

Case VI.—Sick for three years—hæmoptysis the first sign.

From February 17 to June 6, there were fifteen exami-

nations of the sputum, with positive results in twelve. The bacilli were always very few until the last examination, when the number observed increased very greatly, but with no corresponding increase in the temperature. For three months this patient's temperature has been sub-normal much of the time. (Chart VI.)

Case VII.—Sick one year—hæmoptysis the first sign.

From April 20 to June 3, four examinations were made, and very many bacilli were found in every case. This patient's temperature curve was pretty constantly high.

Case VIII.—Cough for one year.

From May 19 to June 3, three examinations were made, with bacilli in diminishing numbers; the temperature upon the days of the examinations being less each time also.

Case IX.—Cough for two years.

From May 19 to June 3, three examinations were made, with very many bacilli in every case. The temperature, however, showed no exact correspondence.

Case X.—Cough and hæmoptysis for ten years.

From February 17 to June 3, fifteen examinations were made, with positive results in six only—and in these the bacilli were always seen in but very small numbers. The temperature of this patient has been for weeks at a time within half a degree of normal.

Case XI.—This was a case of pleurisy which was examined for comparison.

From March 14 to May 19, seven examinations were made, with negative results in every case.

A comparison of the charts tends to show that there is only a very general correspondence between the numbers of the bacilli and the height or variations of the fever line. A large number of bacilli does not necessarily mean a high temperature. The fever curve of each patient varies somewhat, and has a general average of its own, sometimes a very high one and sometimes entirely the opposite. It is

with this average range of temperature in the special case, that the number of the bacilli must be compared; and it is only by this observation of special cases that the information obtained is of value. It is also shown that a continued examination of the sputum for weeks at a time may be necessary before the absence of the bacilli can be definitely assumed—as is shown in Case V., where six successive examinations were made before they were detected. In rapid cases, with free expectoration, there are enormous numbers of the bacilli to be found. The characteristics of the sputum also seem to be something of a guide to the number of bacilli that one may expect to find. If it is largely mucous, with but a few yellowish nodules in it, bacilli will only be found in these nodules; and then, possibly, only in small numbers. If, however, the sputum be of a more purulent fluid character, the bacilli will probably be present in great numbers, whatever portion is examined.

The result of all the work that has been done upon this subject may be summed up as follows:

I.—A staff-shaped micro-organism exists, in all forms of the tuberculous process, and its presence has been demonstrated in them.

II.—It is more abundant in the rapid than in the slow forms of the process.

III.—Its specific nature as the cause of tuberculosis is claimed by Koch on the ground of his observations.

IV.—Its specific character has not been successfully refuted by trustworthy observations.

V.—Its value as diagnostic evidence of tuberculosis is very great; although its absence cannot be considered as excluding that process.

The only observer who has thus far attempted the repetition of Koch's cultivation experiments, is Prof. Feltz (50), of Nancy, who has announced the complete failure of his

work. The manipulation is such, however, that more than one failure must occur to upset the testimony of complete and repeated successes.

TABLE OF REFERENCES IN THE PAPER.

1. R. Koch.—Berlin. Klin. Woch., April 10, 1882. Baumgarten.—Centralblatt für die Med. Weis., No. 25, 1882.
2. Villemin.—Etudes sur Tuberculose. Paris, 1868.
3. Klebs.—Prager Med. Woch., Nos. 42, 43, 1877.
4. Schüller.—Die Scrophulöse und Tuberculöse Gelenkslerden, 1880.
5. Toussaint.—Comptes Rendus, 1881.
6. Aufrecht.—Pathologische Mitheilungen, Magdeburg, 1881.
7. Machiafara and Celli.—Gazzette degli Ospit., Oct. 29, 1882.
8. Formad.—Phil. Med. Times, Nov. 18, 1882.
9. Balmer und Fräntzel.—Berliner Klin. Woch., No. 45, 1882.
10. Hiller.—Zeitschrift für die Klin. Med., v. s. 638.
11. Schmidt.—Chicago Med. Journal and Examiner, Dec. 1882.
12. Hirschfelder.—N. Y. Med. Record, Jan. 6, 1883.
13. Ransome.—British Med. Journal, Dec. 16, 1882.
14. Balogh.—Wiener Med. Woch., No. 51, 1882.
15. Koryani.—Wiener Med. Woch., No. 51, 1882.
16. Guttman.—Berliner Klin. Woch., No. 52, 1882.
17. D'Espine.—Révue Méd. de la Science Romaine, Dec. 1882.
18. Lichtheim.—Fortschritte der Med., No. 1, 1883.
19. Chiari.—Wiener Med. Presse, Jan. 7, 1883.
20. Heron.—British Med. Journal, Jan. 17, 1883; Lancet, Feb. 3, 1883.
21. Smith.—British Med. Journal, Jan. 20, 1883.
22. Pfeiffer.—Berliner Klin. Woch., No. 3, 1883.
23. Babés.—Société d'Anat., Paris, Jan. 26, 1883.
24. Crämer.—Erlanger Phys. Med. Sitzb., Dec. 11, 1882.
24a. Menche.—Verein für Natur—und Heilkunde am Jan. 22, 1883.
25. Fränkel.—Berliner Klin. Woch., No. 4, 1883.
26. Dreschfeld.—British Med. Journ., Feb. 17, 1883.
27. Ziehl.—Deutsche Med. Wochenschrift, No. 5, 1883.
28. Rosenstein.—Centralblatt für die Med. Weisensch., Feb. 3, 1883.
29. West.—London Path. Soc., Feb. 6, 1883.
30. Williams.—Med. Soc. of London, Feb. 12, 1883.
31. Dettweiler und Meissen.—Berlin. Klin. Woch., Nos. 7 and 8, 1883.
32. Spina.—Studien über Tuberkulöse, Wien., 1883.
33. Koch.—Deutsche Med. Wochenschrift, No. 10, 1883.
34. Cutter.—Am. Med. Weekly, 1882.
35. Gregg.—In letter to Koch.
36. Sternberg.—Med. News, No. 1, 1882.
37. Beneke.—Die erste Ueberwinterung auf Nordenay, Norden, 1882.
38. Gaffky.
39. Schottelius. Virchow's Archiv., bd. xci. heft i.
40. Demme.—Berlin. Klin. Woch., No. 15, 1883.
41. Purser.—Dublin Med. Journ., March, 1883.
42. Prudden.—N. Y. Med. Record, April 14, 1883.
43. Cheyne.—Practitioner, April, 1883.

44. Ransome.—British Med. Journ., April 14, 1883.
44a. Gibbes' Method.—British Med. Journal, Oct. 14, 1882.
45. Cornil.—Gazette Hebdomadaire, April 27, 1883.
46. Ballagi.—Wiener Med. Presse, No. 17, 1883.
47. Frantzel.—Deutscher Med. Woch., No. 17, 1883.
48. Spina.—Wien. Med. Presse, May 13 and 20, 1883.
49. Klebs.—Virchow's Arch. f. Exper. Path. und Pharm., bd. 17, s. 51.
50. Feltz.—Gazette Hebdomadaire, March 2, 1873.

CHARTS.

The upper curve represents the temperature on the day of the examination.

The lower curve is a diagrammatic representation of the number of the bacilli found at each examination.

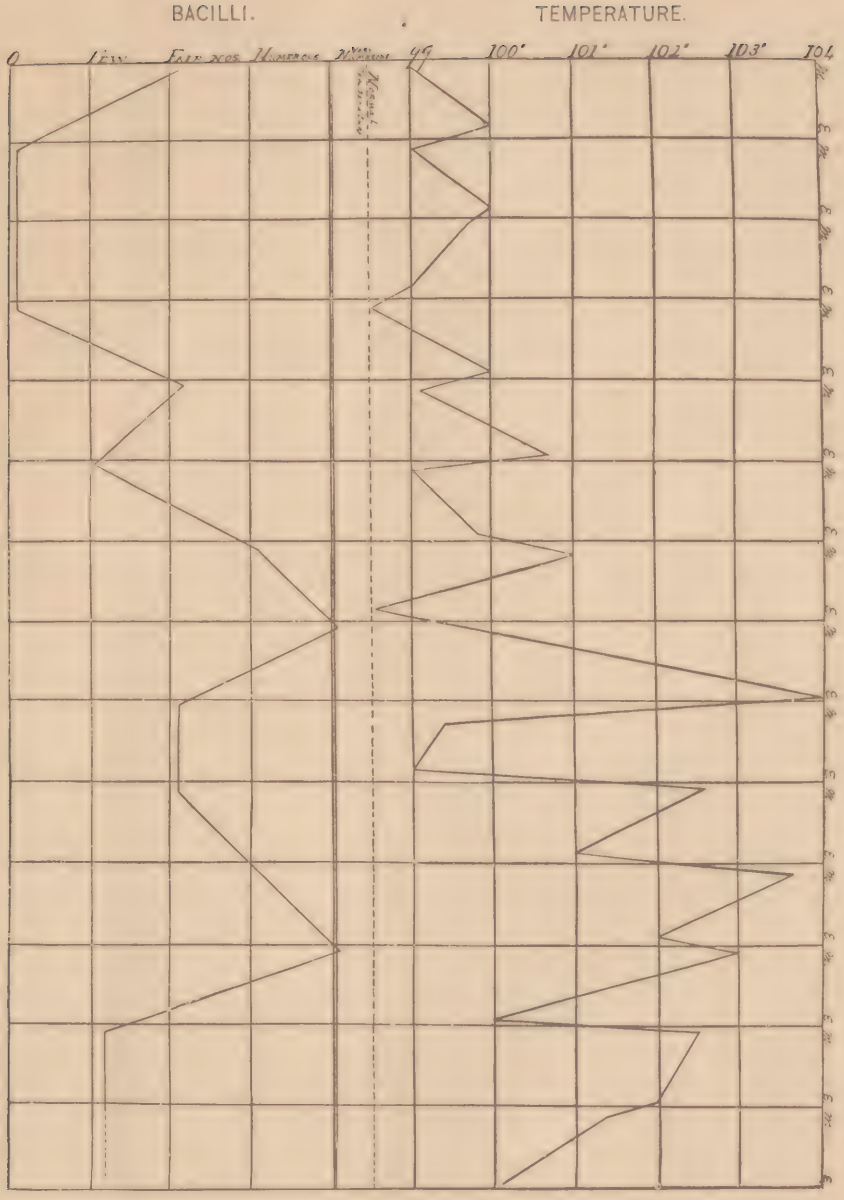
BACILLI.
TEMPERATURE.
0
Few.
Numerous
Normal
99
100°
101°
102°
103°
104

CHART I.

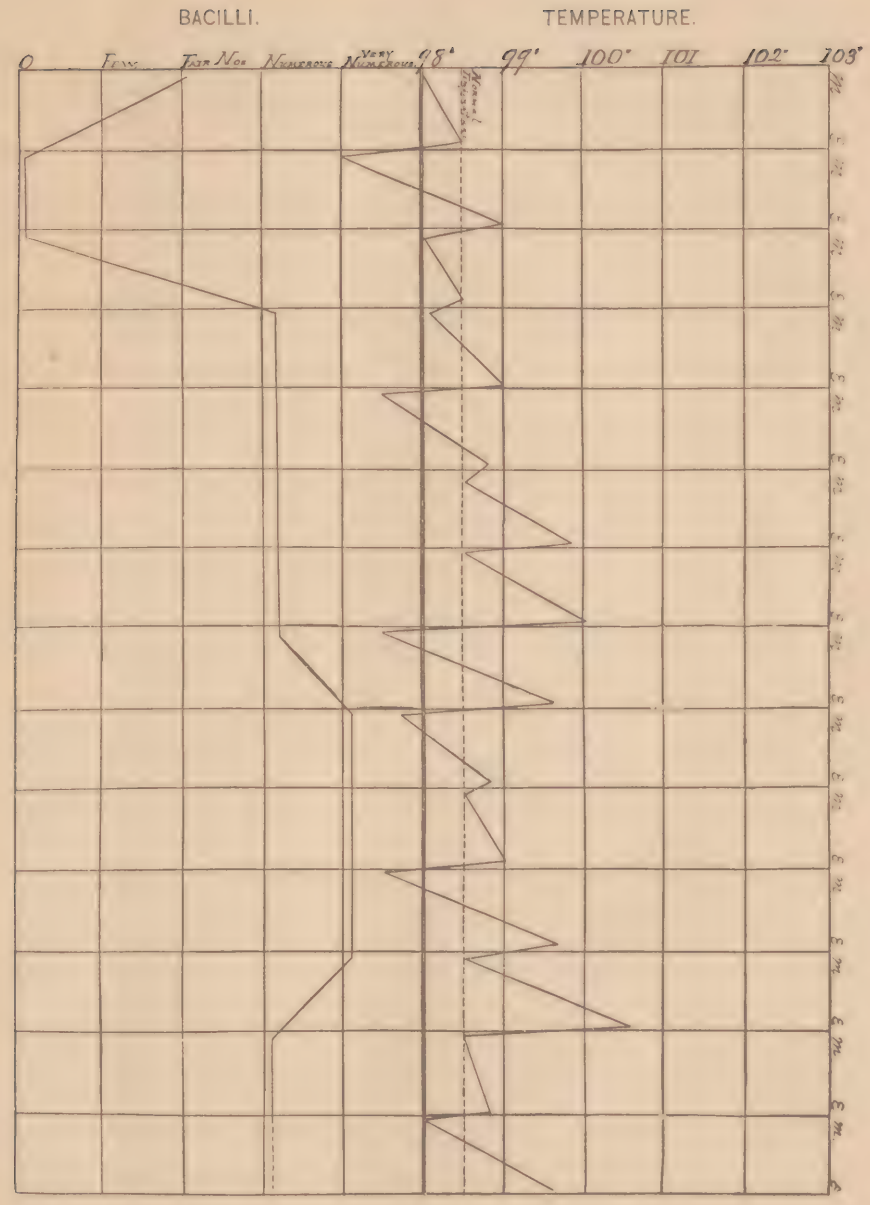
BACILLI.
TEMPERATURE.
0
Few
Too Many
Numerous
Very Numerous
98°
99°
100°
101
102°
103°
Normal Temperature

CHART II.

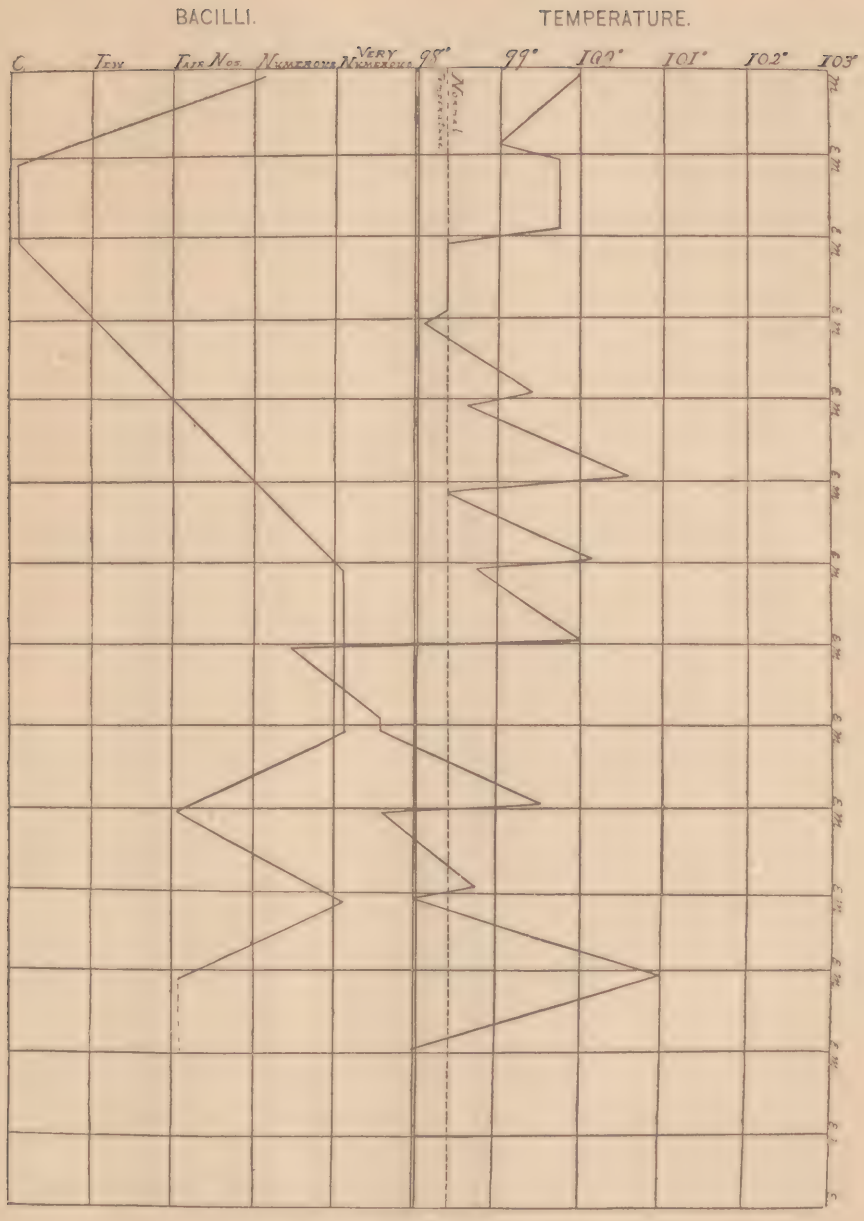
BACILLI.
TEMPERATURE.
C.
Few
Fair Nos.
Numerous
Very Numerous
98°
99°
100°
101°
102°
103°
Normal Temperature
P.M.
6 P.M.
7 P.M.
8 P.M.
9 P.M.
10 P.M.
11 P.M.
12 P.M.
1 A.M.
2 A.M.
3 A.M.
4 A.M.
5 A.M.
6 A.M.
7 A.M.
8 A.M.
9 A.M.
10 A.M.
11 A.M.
12 A.M.
1 P.M.
2 P.M.
3 P.M.
4 P.M.
5 P.M.

CHART IV.

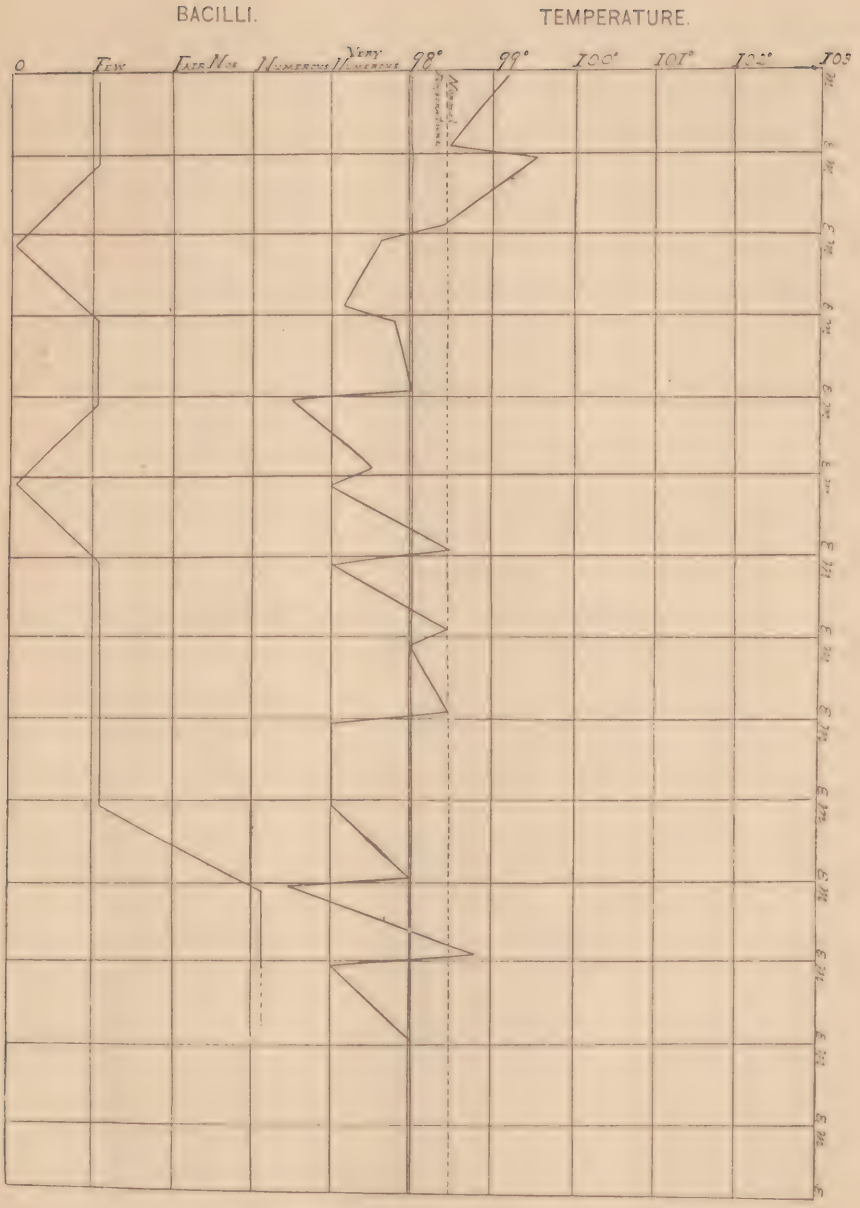
BACILLI.
TEMPERATURE.
0
Few
Int. Nos
Numerous
Very Numerous
98°
99°
100°
101°
102°
103°

CHART V.

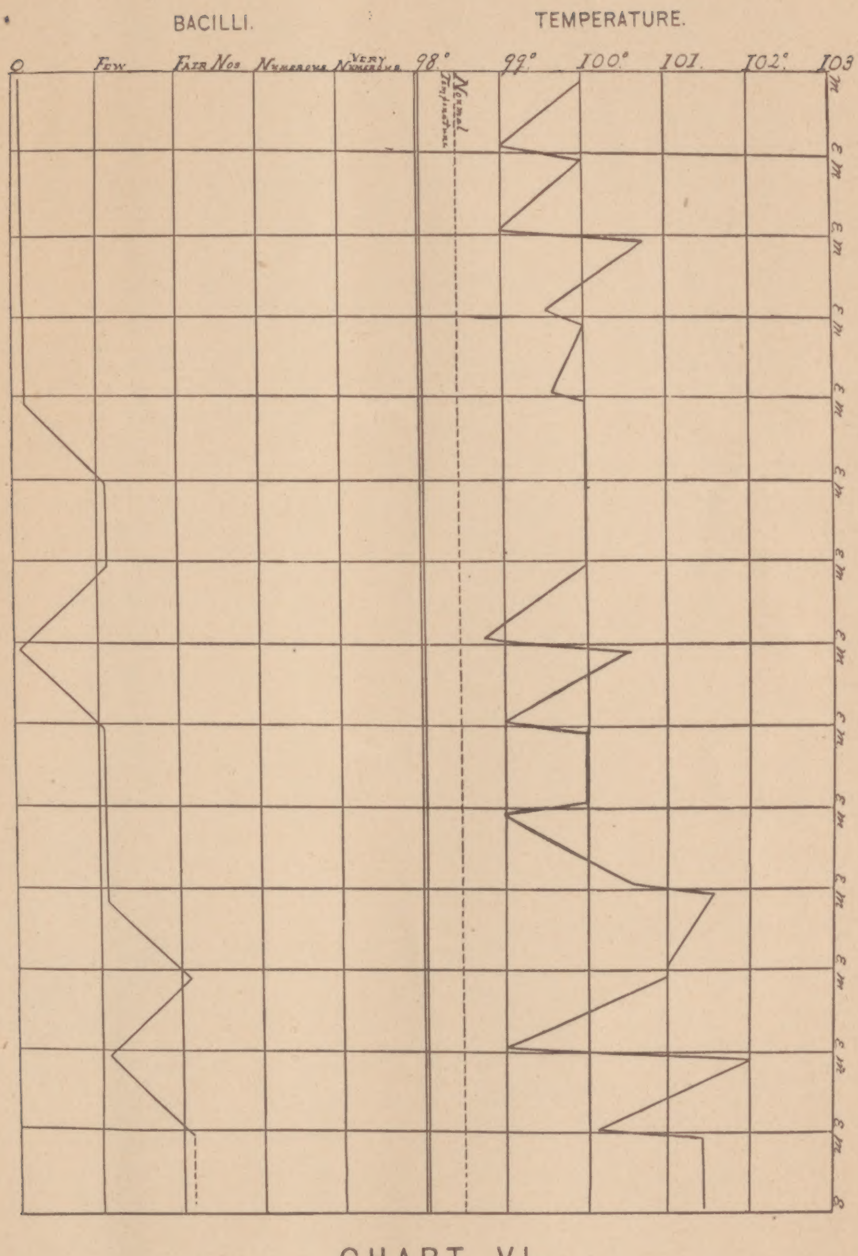
BACILLI.
TEMPERATURE.
0
Few
Fair Nos
Numerous
Very Numerous
98°
99°
100°
101.
102°
103
Normal Temperature

CHART VI.